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| EXAMINER |
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| ART UNIT | PAPER NUMBER |
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| 1647 | 8 |

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Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/712,142 | EBNER ET AL. | |
| | Examiner | Art Unit | |
| | David S Romeo | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *7,14-17 and 19-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-13 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-23* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,4,5* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

## DETAILED ACTION

Applicant's election with traverse of group I, claims 1-13, 18, and the nucleotide sequence that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that groups I-VI should be examined together, the searches of all sequences of group I would overlap, the examiner has not addressed MPEP § 803.04. This is not found persuasive because upon further consideration polynucleotides encoding full-length, full-length minus the N-terminal methionine, mature, and 50 mer polypeptides have been rejoined. This is not found persuasive because an application may properly be required to be restricted to one of two or more claimed invention if they are able to support separate patents and they are either independent (MPEP § 806.04 - § 806.04 (j)) or distinct (MPEP § 806.05 - § 806.05(i)). Groups I-VI are distinct for the reasons given in the Office action mailed June 28, 2002 (Paper No. 6). Furthermore, separate classification (i.e., class and subclass) of distinct inventions is sufficient to establish a prima facie case that the search and examination of the plural inventions imposes a serious burden upon the Examiner. See M.P.E.P. § 803. Such separate classification is set forth in the Office action mailed June 28, 2002 (Paper No. 6). Polynucleotide and polypeptide searches are not coextensive as indicated by their separate classification. Applicant has offered no evidence to rebut this showing. Contrary to Applicants' assertion that any search of the prior art in regard to any one group will reveal whether any prior art exists as to the other groups, a search is directed to references which would render the invention obvious, as well as references directed to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter. This is not found persuasive because MPEP § 803.04 states that up to ten independent and distinct

nucleotide sequences will be examined in a single application without restriction. "One" is "up to ten." Furthermore, the fragments in claim 7 are different proteins and are structurally distinct chemical compounds and are unrelated to one another. The nucleotide sequences encoding them are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Applicants may petition pursuant to 37 CFR 1.181 for examination of additional nucleotide sequences by providing evidence that the different nucleotide sequences do not cover independent and distinct inventions.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7, 14-17, 19-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claims 1-6, 8-13, 18 are being examined only to the extent that they are directed polynucleotides encoding full-length, full-length minus the N-terminal methionine, mature, and 50 mer polypeptides.

The application is not fully in compliance with the sequence rules, 37 C.F.R. § 1.821-1.825. Specifically, the specification fails to recite the appropriate sequence identifiers at each place where a sequence is discussed. Specifically, Figure 2 is missing a SEQ ID NO: for CTFG-3. This is not meant to be an exhaustive list of places where the specification fails to comply with the sequence rules. The specification has not been checked to the extent necessary to

determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. The application cannot issue until it is in compliance. Nucleic acid sequences with 10 or more nucleotides, at least 4 of which are specifically defined, must comply with the sequence rules. Amino acid sequences with 4 or more residues, at least 4 of which are specifically defined, must comply with the sequence rules. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the "Sequence Listing." Applicant may bring the figure(s) into compliance by amending either the figure(s) or the "Brief Description of the Drawings" to recite the appropriate sequence identifier.

Correction is required.

***Information Disclosure Statement***

References AS and AT on the information disclosure statement (IDS) filed May 31, 2002 (Paper No. 5) have not been considered because the relevance of the sequences disclosed in the references to the present sequences is impossible to ascertain in the absence of an alignment.

The GenBank entries on the IDS have been considered to the extent possible, but a residue by residue comparison has not been done.

***Claim Rejections - 35 USC § 101***

Claims 1-6, 8-13, 18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The specification discloses a protein having the amino acid sequence of SEQ ID NO: 2 and discloses that the protein can be made by protein synthesis techniques well known in the art. There is no description of the chemical, physical, or biological properties for the protein other than the sequence. The disclosed utilities associated with the claimed protein are based upon its homology with CTGF-1. CTGF-3, SEQ ID NO:2, is about 44% identical and about 59% similar to human CTGF-1 (page 7, lines 27-30).

Henikoff (AT, cited by Applicants) teaches that shared modules in proteins are to be used as guides for further research. Furthermore, Henikoff expresses uncertainty about gene classification (page 609, column 1, paragraph bridging columns 1-2) and family relationships are complex (paragraph bridging pages 613-614); computer-based tools may not be the solution (page 614, column 1, full paragraph 1). It is noted that the instant specification fails to correlate a specific function of CTGF-3 with any given module of CTGF-3, or even with the entire protein.

Additionally, there is no art of record that discloses or suggests any activity for the claimed protein. Therefore there is no well-established utility. The instant application has provided a description of a single DNA molecule comprising the nucleotide sequence of SEQ ID NO:1, that encodes a protein, connective tissue growth factor-3 (CTGF-3), having the amino acid sequence of SEQ ID NO:2. The instant application does not disclose a specific biological role of CTGF-3 or its significance. Although connective tissue growth factors belong to the CCN peptide family, most of the members of the CCN family lack a clear biological activity and the development of biological assays for these molecules is problematic. See Grotendorst (AS, cited by Applicants), page 172, paragraph bridging columns 1-2 and page 174, column 1, full

paragraph 1. Grotendorst (published in 1997) teaches that progress in understanding the functions of the CNN family of peptides has been limited in spite of the cloning of cef/10 (identified in 1989), cyr61 (identified in 1990), Fisp12 (identified in 1991), and nov (identified in 1992) (page 174, column 2, full paragraph 1, and the references cited therein). It is noted that although CTGF, cef/10, cyr61, Fisp12, and nov belong to the same family of structurally related proteins, Grotendorst does not ascribe a biological role, function, or activity based on the structural relatedness.

Further experimentation is necessary to attribute a utility to the claimed protein. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated in the context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful completion.").

Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. There is little doubt that after complete characterization, CTGF-3 will be found to have a patentable utility. This further characterization, however, is part of the act of invention, and until it has been undertaken the claimed invention is incomplete. In the absence of a knowledge of the biological significance of this protein, there is no immediately obvious patentable use for it. To employ the polynucleotides and polypeptides of the instant invention in order to raise antibodies, which antibodies are useful for detecting the polypeptide, for the diagnosis and prognosis of connective tissue related disorders, therapeutically, or for chromosome identification is clearly to use them

as the object of further research which is a non-patentable utility. Furthermore, the specification lacks evidence supporting these utilities. Assertions that the CTGF-3 polypeptide or polynucleotide have utility for the above purposes requires sufficient support in the application's disclosure. The patentability of CTGF-3 polypeptides and polynucleotides will require more that the mere allegation of utility.

Claims 1-13, 18 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 9-13, 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the deposit of ATCC Deposit No. 97756. While the specification provides enough information for one of skill in the art to produce a polynucleotide comprising a coding sequence with the same or similar properties as, reproduction of an identical polynucleotide is a highly unpredictable event. Because it does not

appear that ATCC Deposit No. 97756 is known and publicly available or can be reproducibly isolated form nature without undue experimentation and because the claims require the use of ATCC Deposit No. 97756, a suitable deposit of the clones is required for patent purposes.

Applicants referral to the deposit of ATCC Deposit No. 97756 at paragraph bridging pages 3-4 is insufficient to ensure that all of the conditions of 37 CFR § 1.801-1.809 have been met.

If the deposit was made under the provision of the Budapest Treaty, filing of an affidavit or declaration by applicants or assignees, or a statement by an attorney of record over his or her signature and registration number, stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository, is required. This requirement is necessary when a deposit is made under the provisions of the Budapest Treaty as the treaty leaves these specific matters to the discretion of each State. Amendment of the specification to recite the date of the deposit and the complete name and address of the depository, and amendment of the claims to refer to the accession number, is required. In addition, claims reciting the deposited material must be amended to include the depository accession number of the deposited material.

Furthermore, unless the deposit was made at or before the time of filing, a declaration under 37 CFR 1.132 is necessary to construct a chain of custody. The declaration, executed by a person in a position to know, should identify the deposited clones by its depository accession

number, establish that the deposited clones are the same as that described in the specification and establish that the deposited clone was in applicants' possession at the time of filing.

The new address for the ATCC, effective March 23, 1998, is American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209.

Claims 1, 5, 6, 8-10, 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polynucleotides having at least 95% sequence identity with a genus of all polynucleotides encoding the amino acid sequence of SEQ ID NO: 2, to polynucleotides that hybridize under stringent conditions to a genus of all polynucleotides encoding the amino acid sequence of SEQ ID NO: 2, to polynucleotides comprising a nucleotide sequence encoding the amino acid sequence of an epitope bearing portion of SEQ ID NO: 2, to polynucleotides comprising a 50 nucleotide fragment of SEQ ID NO: 1, and to polynucleotides encoding a substituted amino acid sequence of SEQ ID NO: 2. The claims do not require that the polynucleotide or polypeptide possess any particular function, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides encoding a genus of polypeptides that is defined only by some level of partial sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus.

The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial or variable structure. There is no recitation of a structure/function correlation. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only polynucleotides comprising the nucleotide sequence set forth in SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1, 5, 6, 8-10, 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to polynucleotides having at least 95% sequence identity with a genus of all polynucleotides encoding the amino acid sequence of SEQ ID NO: 2, to polynucleotides that hybridize under stringent conditions to a genus of all polynucleotides encoding the amino acid sequence of SEQ ID NO: 2, to polynucleotides comprising a nucleotide sequence encoding the amino acid sequence of an epitope bearing portion of SEQ ID NO: 2, to polynucleotides comprising a 50 nucleotide fragment of SEQ ID NO: 1, and to polynucleotides

encoding a substituted amino acid sequence of SEQ ID NO: 2. There are no functional limitations in the claims.

The claim encompasses an unreasonable number of inoperative embodiments, which the skilled artisan would not know how to use. While the specification suggests that CTGF-3 is a member of the growth factor superfamily and may posses properties typical of other growth factor superfamily members, it is unclear what properties the claimed variant polynucleotides and polypeptide may possess. Knowledge of one CTGF polypeptide's structure and function does not provide predictability about function of a structurally related polypeptide, even within the same class.

There are no working examples of polynucleotides or polypeptides less than 100% identical to CTFG-3. The skilled artisan would not know how to use non-identical polynucleotides and polypeptides on the basis of teachings in the prior art or specification unless they exhibited the same activity as CTGF-3 polynucleotides and polypeptides. The specification does not provide guidance for using CTGF-3 polynucleotides and polypeptides related to (i.e., variant) but not identical to SEQ ID NO: 1 which do not have a single specific disclosed activity shown for CTGF-3 polynucleotides or polypeptides. The claims are broad because they do not require the claimed polynucleotide to be identical to the disclosed sequence and because the claims have no functional limitation.

The specification does not teach the skilled artisan how to use the claimed polynucleotides encoding CTFG-3 for purposes unrelated to or divorced from a biological activity. Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polynucleotides.

Henikoff (AT, cited by Applicants) teaches that shared modules in proteins are to be used as guides for further research. Furthermore, Henikoff expresses uncertainty about gene classification (page 609, column 1, paragraph bridging columns 1-2) and family relationships are complex (paragraph bridging pages 613-614); computer-based tools may not be the solution (page 614, column 1, full paragraph 1). The instant application does not disclose a specific biological role of CTGF-3 or its significance. Although connective tissue growth factors belong to the CCN peptide family, most of the members of the CCN family lack a clear biological activity and the development of biological assays for these molecules is problematic. See Grotendorst (AS, cited by Applicants), page 172, paragraph bridging columns 1-2 and page 174, column 1, full paragraph 1. Grotendorst (published in 1997) teaches that progress in understanding the functions of the CNN family of peptides has been limited in spite of the cloning of cef/10 (identified in 1989), cyr61 (identified in 1990), Fisp12 (identified in 1991), and nov (identified in 1992) (page 174, column 2, full paragraph 1, and the references cited therein). It is noted that although CTGF, cef/10, cyr61, Fisp12, and nov belong to the same family of structurally related proteins, Grotendorst does not ascribe a biological role, function, or activity based on the structural relatedness.

Due to the large quantity of experimentation necessary to determine an activity or property of CTFG-3, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity, and the breadth of the claims which fail to recite particular biological activities and also embrace a broad class of structural fragments and variants, undue

experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

For these reasons, which include the complexity and unpredictability of the nature of the invention and art in terms of the diversity of the claimed polynucleotides and lack of knowledge about function(s) of encompassed polynucleotides and polypeptides structurally related to CTGF-3, the lack of direction or guidance for using polynucleotides and polypeptides that are not identical to CTGF-3, and the breadth of the claims encompassing structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is unclear if the antecedent basis for the term "or a subfragment thereof" is the claimed polynucleotide or SEQ ID NO: 11. A single nucleotide is a subfragment. In the case where the antecedent basis for the term is SEQ ID NO: 11 the present specification has not enabled a polynucleotide that does not contain a single nucleotide of SEQ ID NO: 11.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 4, 13 are indefinite because they recite the term "connective tissue growth factor-3". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "connective tissue growth factor-3" an artisan cannot determine what additional or material structural or functional limitations are placed upon a claim by the presence of this element.

Claims 1, 3-6, 9-13, 18 are indefinite because they recite the term "connective tissue growth factor-3". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "connective tissue growth factor-3" an artisan cannot determine what additional or material structural or functional limitations are placed upon a claim by the presence of this element.

Claims 1, 4-6, 9-13, 18 are indefinite because they recite the term "mature". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "mature" an artisan cannot determine what additional or material structural or functional limitations are placed upon a claim by the presence of this element.

Claim(s) 5 is indefinite over the recitation of "stringent hybridization conditions" because stringency varies according to the hybridization conditions and the particular hybrid under study. See Sambrook (u8), page 9.50, paragraph 9. The specification fails to precisely define "stringent conditions". Any degree of stringency is embraced by the claims. One of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. The metes and bounds are not clearly set forth.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear if the antecedent basis for the term "or a subfragment thereof" is the claimed polynucleotide or SEQ ID NO: 11. It is unclear if the fragment comprises at least 50 contiguous nucleotides of nucleotides 1-231 of SEQ ID NO: 1, or if the fragment is at least 50 nucleotides long irrespective of nucleotide composition. The metes and bounds are not clearly set forth.

***Claim Objections***

Claims 5, 6 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. A polynucleotide that hybridizes to (a), (b), (c), (d), (e), or (f) of claim 1 fails to further limit the isolated nucleic acid molecule of claim 1. A polynucleotide encoding an epitope bearing portion of (a), (b), (c), (d), (e), or (f) of claim 1 fails to further limit

the isolated nucleic acid molecule of claim 1. Furthermore, claims in dependent form shall be construed to include all the limitations of the claim incorporated by reference into the dependent claim, but dependent claims 5, 6 include only a portion of the limitations of the claim incorporated by reference into the dependent claims.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by Purchio (AL1, cited by Applicants). It is unclear if the antecedent basis for the term "or a subfragment thereof" is the claimed polynucleotide or SEQ ID NO: 11. A single nucleotide is a subfragment. Purchio teaches an isolated nucleic acid molecule comprising a polynucleotide having the sequence of a subfragment of a nucleotide sequence of a fragment of the sequence comprising nucleotides 1-231 of SEQ ID NO: 1, wherein said fragment comprises at least 50 contiguous nucleotides, and said isolated nucleic acid molecule does not have the sequence shown in SEQ ID NO: 11 (Figure 1; page 7, full paragraph 1). Insofar as the isolated nucleic acid molecule was cloned, then Purchio also discloses the complement thereof.

Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Grotendorst (AA1, cited by Applicants) in view of Benjamini (v8). Grotendorst teaches an isolated nucleic acid

molecule encoding the amino acid sequence "dvrlps" (Example 4) which is identical to the amino acid sequence of residues 137-142 of the present application's SEQ ID NO: 2. Various studies indicate that the size of an epitope is approximately equivalent to 5-7 amino acids. See Benjamini, page 40. Claim 6 fails to further limit the subject matter of claim 1. Accordingly, Grotendorst teaches an isolated nucleic acid molecule comprising a polynucleotide which encodes the amino acid sequence of an epitope-bearing portion of a CTFG-3 polypeptide having an amino acid sequence in (a), (b), (c), (d), (e), or (f) of claim 1.

Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Perbal (n8). Claim 5 fails to further limit the subject matter of claim 1. The metes and bounds of "stringent hybridization conditions" are not clearly set forth. Nucleotides 9-758 of the present application's SEQ ID NO: 1 encode the amino acid sequence of the present application's SEQ ID NO: 2. Perbal discloses an isolated nucleic acid molecule that is 56% identical to nucleotides 9-758 of the present application's SEQ ID NO: 1 (page 26), as indicated below:

```
  Query Match             23.5%;  Score 176.4;  DB 14;  Length 684;
  Best Local Similarity   57.5%;  Pred. No. 7.7e-27;
  Matches  359;  Conservative    0;  Mismatches  256;  Indels    9;  Gaps    2;

Qy      93 ctgcccctggccacctccccgatgcccgctgggagtacccctggtgctggatggctgtgg 152
           |||||||  |   || || || ||| | | |||||| |||   |||||||| |||||  |
Db      12 ctgccccgcggagccgccgcgctgcgccccgggagtgcccgccgtgctggacggctgccg 71

Qy     153 ctgctgccgggtatgtgcacggcggctgggggagccctgcgaccaactccacgtctgcga 212
           |||||||| ||| || || |||| ||  || |||  ||||  ||  || |    ||||||
Db      72 ctgctgcctggtgtgcgcccggcagcgcggcgagagctgctcccctctgctgccctgcga 131

Qy     213 cgccagccagggcctggtctgccagcccggggcaggacccggtggccgggggccctgtg 272
           ||  |||   |||||   |||| | | |||  | |    ||| ||| | |  | | | ||
Db     132 cgagagcggcggcctctactgcgaccgcggccccgaggacggcggcggcgccggcatctg 191

Qy     273 cctcttggcagaggacgacagcagctgtgaggtgaacggccgcctgtatcgggaagggga 332
           | |  ||   || |  ||   || ||| | | |  | ||     | || ||  | |||||
Db     192 catggtgctggaagggga---caactgcgtgttcgatgggatgatttaccgcaacgggga 248

Qy     333 gaccttccagccccactgcagcatccgctgccgctgcgaggacggcggcttcacctgcgt 392
           ||| |||||||||  |||||    ||  |||  ||||  ||||||     ||   ||| |
```

```
Db    249 gacgttccagcccagctgcaagtaccagtgcacctgccgggacgggcagatcgggtgcct 308

Qy    393 gccgctgtgcagcgaggatgtgcggctgcccagctgggactgcccccacccccaggagggt 452
          ||| |  |||| |  ||   ||| ||| ||| ||   |||||||||  |||  ||| | |
Db    309 gccccgctgcaacctgggcctgctgctccccggccccgactgccccttcccgcggaagat 368

Qy    453 cgaggtcctgggcaagtgctgccctgagtgggtgtgcggcc------aaggaggggact 506
          ||| ||||  ||  ||||||||    ||||||||||||  ||      | | || |   ||
Db    369 cgaagtccccggagagtgctgcgagaagtgggtgtgcgaccccagggatgaagtgctcct 428

Qy    507 ggggacccagccccttccagcccaaggaccccagttttctggccttgtctcttccctgcc 566
          |||   |    |  |  | ||  |  |||   ||    |        |
Db    429 gggaggctttgctatggctgcatacagacaggaggccacacttgggatagacgtgtctga 488

Qy    567 ccctggtgtcccctgcccagaatggagcacggcctggggaccctgctcgaccacctgtgg 626
            | ||| |   ||    |||  ||  || |  ||| |  | || || |  | ||||||
Db    489 ttcaagtgccaattgtattgaacagacaacagaatggagtgcttgttccaaaagctgtgg 548

Qy    627 gctgggcatggccacccgggtgtccaaccagaaccgcttctgccgactggagacccagcg 686
            |||||  |  | |||||  ||  |||||   || |    ||     ||| ||  |||
Db    549 aatgggcttttctacccgtgttaccaacagaaatcagcagtgtgagatggtgaagcagac 608

Qy    687 ccgcctgtgcctgtccaggccctg 710
           || || |||  ||   || ||  ||
Db    609 acgactttgcatgatgagaccttg 632
```

The nucleic acid molecule or its complement would hybridize under stringent hybridization conditions to a polynucleotide having a nucleotide sequence identical to a nucleotide sequence in (a), (b), (c), (d), (e), or (f) of claim 1.

## *Conclusion*

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306
AFTER FINAL (703) 872-9307

IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
NOVEMBER 3, 2002